

What is claimed is:

Sub a1 1. A method of making a transgenic fusion protein comprising providing a transgenic animal which includes a transgene which provides for the expression of the fusion protein; allowing the transgene to be expressed; and, recovering the fusion protein, from the milk of the transgenic animal.

10 2. The method of claim 1, wherein the fusion protein includes an immunoglobulin-subunit and an enzyme.

15 3. The method of claim 1, wherein the fusion protein includes a first member fused to a second member and the first member includes the subunit of a targeting molecule and the second member encodes a cell toxin.

20 4. The method of claim 1, wherein the fusion protein includes a subunit of an Ig specific for a tumor antigen .

5. The method of claim 4, wherein the tumor antigen is from the group carcinembryonic antigen (CEA), a transferring receptor, TAG-72, an epidermal growth factor receptor.

25 6. The method of claim 1, wherein the fusion protein includes an Rnase.

7. The method of claim 6, wherein the Rnase is RnaseA.

Sub a2 8. The method of claim 1, wherein the fusion protein includes angiogenin.

9. The method of claim 1, wherein the fusion protein includes carboxypeptidase B enzyme.

Sub 3

10. The method of claim 1, wherein the fusion protein is made in a mammary gland of the transgenic mammal.

11. The method of claim 1, wherein the fusion protein is secreted into the milk of 5 a transgenic mammal at concentrations of at least about 0.5 mg/ml or higher.

12. The method of claim 1, wherein the fusion protein is secreted into the milk of a transgenic mammal at concentrations of at least about 1.0 mg/ml or higher.

10 13. The method of claim 1, the immunoglobulin subunit of a fusion protein is a humanized antibody.

14. The method of claim 1, wherein the transgene encoding the transgenic fusion protein is a nucleic acid construct which includes:

15 (a) optionally, an insulator sequence;
(b) a mammary epithelial specific promoter;
(c) a nucleotide sequence which encodes a signal sequence which can direct the secretion of the fusion protein, e.g. a signal from a milk specific protein;
(d) optionally, a nucleotide sequence which encodes a sufficient portion of the 20 amino terminal coding region of a secreted protein, e.g. a protein secreted into milk, to allow secretion, e.g., in the milk of a transgenic mammal, of the fusion protein;
(e) one or more nucleotide sequences which encode the fusion protein; and
(f) optionally, a 3' untranslated region from a mammalian gene.

25 15. An isolated nucleic acid construct, which includes:
(a) optionally, an insulator sequence;
(b) a mammary epithelial specific promoter;
(c) a nucleotide sequence which encodes a signal sequence which can direct the secretion of the fusion protein, e.g. a signal sequence from a milk specific protein;

(d) optionally, a nucleotide sequence which encodes a sufficient portion of the amino terminal coding region of a secreted protein, e.g. a protein secreted into milk, to allow secretion, e.g., in the milk of a transgenic mammal, of fusion protein;

5 (e) one or more nucleotide sequences which encode a fusion protein as described in claim 1; and

(f) optionally, a 3' untranslated region from a mammalian gene, e.g., a mammary epithelial specific gene, (e.g., a milk protein gene).

In another aspect, the invention features, a pharmaceutical or nutraceutical composition having an effective amount of fusion protein, e.g., an immunoglobulin-enzyme 10 fusion protein as described herein, and a pharmaceutically acceptable carrier.

In a preferred embodiment, the composition includes milk.

15 *b 24* *16* *18 human* A transgenic animal which includes a transgene that encodes a fusion protein

described in claim.

16. *17* The transgenic animal of claim 15, which can secrete the fusion protein into its milk at concentrations of at least about 0.5 mg/ml or higher.

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